UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

ALLERGAN, INC., Plaintiff, v. TEVA PHARMACEUTICALS USA, INC., AKORN, INC., MYLAN PHARMACEUTICALS INC., and MYLAN INC., Defendants.	Civil Action No. 2:15-cv-1455-WCB (Consolidated) LEAD CASE JURY TRIAL DEMANDED

DEFENDANTS' MOTION FOR PARTIAL SUMMARY JUDGMENT OF NONINFRINGEMENT

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I. INTRODUCTION

Restasis®, the purported commercial embodiment of the patents-in-suit, has been approved by FDA for one indication, and one indication alone: to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca ("KCS"). FDA approved Restasis® to increase tear production after concluding that the results of Allergan's Phase 2 and Phase 3 clinical trials failed to show efficacy in treating moderate to severe KCS and dry eye. Rather, the data showed that Schirmer scores, a method of measuring tear production, only demonstrated that Restasis® increased tear production. Accordingly, Restasis® is not FDA-approved to treat dry eye or KCS. Nor is Restasis® FDA-approved to restore tear production to some prior healthy state.

Yet, Allergan contends that Defendants infringe claims that recite methods of use or efficacy conditions for treating dry eye or KCS and methods of use or efficacy conditions for restoring tearing to a prior healthy state. Defendants do not and cannot infringe these claims. By statute, Defendants may only seek approval from FDA to market a drug for the same indication that has been FDA-approved based on the Restasis® NDA. Under controlling legal precedent, no Hatch-Waxman defendant can be liable for infringing claims directed to uses that are not FDA-approved. Allergan does not dispute that each Defendants' proposed ANDA label recites the same indication as the Restasis® label. Therefore, Defendants' proposed ANDA products cannot infringe, directly or indirectly, claims that are directed to methods of use and efficacy conditions that are not FDA-approved, *i.e.*, treating dry eye or KCS and restoring tearing.

Accordingly, Defendants[1] request that the Court grant partial summary judgment of noninfringement of claims reciting these unapproved (off-label) uses.[2]

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[1] Moving Defendants include Teva Pharmaceuticals USA, Inc.; InnoPharma, Inc.; Famy Care, Ltd.; Akorn, Inc.; Mylan Pharmaceuticals; and Mylan, Inc.

[2] If the Court were to agree with Defendants on the instant issues, some of the asserted claims, which are directed to the indication on the Restasis® label, *i.e.*, increasing tear production, will remain.

II. STATEMENT OF ISSUES TO BE DECIDED BY THE COURT

1. Whether Defendants are entitled to partial summary judgment of noninfringement of claims 17, 25, and 26 of the '111 patent; claims 13, 14, and 24 of the '162 patent; claims 11 and 18 of the '556 patent; and claims 12, 13, 16, 22, 26, and 27 of the '191 patent because Defendants do not seek FDA-approval for ANDA products for the use or treatment of dry eye, dry eye syndrome, dry eye disease, KCS, or restoring tearing, as claimed.

III. STATEMENT OF UNDISPUTED MATERIAL FACTS

1. On February 24, 1999, Allergan submitted its NDA for Cyclosporine Ophthalmic Emulsion, 0.05% to FDA. Ex.1, AGN_RES0003896-4264 at 923.
2. Each Defendant has filed an ANDA seeking FDA approval to market a Cyclosporin Opthalmic Emulsion, 0.05%, a generic version of Allergan's Restasis® product. Doc. No. 96 at ¶¶ 17, 29, 44, 57.
3. Each Defendant has certified to the '111, '162, '556, '048, and '930 patents under § 505(j)(2)(a)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act, stating that each of the patents-in-suit "is invalid… or will not be infringed" by the generic drug. Doc. No. 96 at ¶¶ 101, 109, 117, 125; Doc. No. 1 in No. 2:16-cv-401 at ¶ 55.
4. At the time Mylan, Teva, Akorn, and InnoPharma certified to the '111, '162, '556, '048, and '930 patents in July 2015, the '191 patent had not yet issued. Doc. No. 96 at ¶¶ 101, 109, 117, 125.
5. The '191 patent issued on February 2, 2016. Ex. 10.
6. Allergan contends that Restasis® is the commercial embodiment of the patents-in-suit. *E.g.*, Ex. 2, Opening Expert Report of Robert Noecker (Mylan) at ¶ 78.[3]

[3] Dr. Noecker, Allergan's expert on infringement, submitted multiple infringement reports, one for each Defendant. These reports each present similar theories of infringement. Therefore, Defendants submit the Opening Expert Report of Robert Noecker Regarding Infringement by Mylan as exemplary of Dr. Noecker's infringement theories as to all Defendants.

7. The "Indications and Usage" section of the Restasis® label states: "RESTASIS® ophthalmic emulsion is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca. Increased tear production was not seen in patients currently taking topical anti-inflammatory drugs or using punctal plugs." Ex. 4, AGN_RES0069704-709 at 705.

8. Allergan alleges that each of Defendants' proposed ANDA products infringe certain claims of the six patents-in-suit: U.S. Patent 8,629,111 ("the '111 patent"); U.S. Patent 8,633,162 ("the '162 patent"); U.S. Patent 8,642,556 ("the '556 patent"); U.S. Patent 8,648,048 ("the '048 patent"); U.S. Patent 8,685,930 ("the '930 patent"); and U.S. Patent 9,248,191 ("the '191 patent") (collectively "patents-in-suit"). Exs. 5-10.

9. Allergan asserts claims against Defendants that recite methods of use or efficacy requirements for the treatment of dry eye, dry eye syndrome, dry eye disease, KCS, or restoring [lacrimal gland] tearing. These claims are

   - Claims 13, 14, and 24 of the '162 patent;
   - Claims 12, 13, 16, 22, 26 and 27 of the '191 patent;
   - Claims 11 and 18 of the '556 patent; and
   - Claims 17, 25, and 26 of the '111 patent.

10. Claims 13 and 14 of the '162 patent depend from claim 1. Claim 1 of the '162 patent recites:

> A method of treating dry eye disease, the method comprising topically administering to the eye of a human in need thereof an emulsion at a frequency of twice a day, wherein the emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, acrylate/C10-30 alkyl acrylate cross-polymer, water, and castor oil in an amount of about 1.25% by weight; and

> wherein the topical ophthalmic emulsion is effective in treating dry eye disease.
>
> Ex. 6.

11. Claim 24 of the '162 patent depends from the method of claim 23, which recites, in part, "[a] method of treating dry eye disease. . . ." *Id.*

12. Claim 12 of the '191 patent depends from claim 1. Claim 1 of the '191 patent states:

> A method of treating dry eye disease, the method comprising topically administering to a human eye in need thereof a first topical ophthalmic emulsion at a frequency of twice a day, wherein the first topical ophthalmic emulsion comprises cyclosporin A in an amount of about 005% by weight, polysorbate 80, acrylate/C10-30 alkyl acrylate cross-polymer, water, and castor oil in an amount of about 1.25% by weight;
>
> wherein the method is therapeutically effective in treating dry eye disease;
>
> wherein the method provides overall efficacy substantially equal to administration of a second topical ophthalmic emulsion to a human eye in need thereof at a frequency of twice a day, the second emulsion comprising cyclosporin A in an amount of about 0.1 % by weight and castor oil in an amount of about 1.25% by weight; and
>
> wherein the method results in substantially no detectable concentration of cyclosporin A in the blood of the human.
>
> Ex. 10.

13. Claim 16 of the '191 patent depends from claim 13. Claim 13 states, in relevant part, "[a] method of enhancing tearing in a human eye . . . wherein the method is therapeutically effective in treating dry eye disease. . . ." *Id.*

14. Claims 22, 26, and 27 of the '191 patent depend from claim 21, which recites, in part, "[a] method of restoring tearing. . . ." *Id.*

15. Claim 11 of the '556 patent depends from claim 1 of that patent, which recites:

> A first topical ophthalmic emulsion for treating an eye of a human, wherein the first topical ophthalmic emulsion comprises cyclosporin A in an amount of

about 005% by weight, polysorbate 80, acrylate/C10-30 alkyl acrylate cross-polymer, water, and castor oil in an amount of about 1.25% by weight; and

wherein the first topical ophthalmic emulsion is therapeutically effective in treating dry eye disease; and

wherein the first topical ophthalmic emulsion provides overall efficacy substantially equal to a second topical ophthalmic emulsion comprising cyclosporin A in an amount of about 0.1% by weight and castor oil in an amount of about 1.25% by weight.

Ex. 7.

16. Claim 18 of the '556 patent depends from claim 13, which is directed to "[a] first topical ophthalmic emulsion for treating an eye of a human . . . wherein the first topical ophthalmic emulsion is therapeutically effective in treating dry eye disease." *Id.*

17. Claim 17 of the '111 patent states "[t]he topical ophthalmic emulsion of claim 13, wherein the topical ophthalmic emulsion is effective in treating kerataconjunctivitis sicca." Ex. 5.

18. Claim 25 of the '111 patent states "[t]he topical ophthalmic emulsion of claim 18, wherein the topical ophthalmic emulsion is therapeutically effective in treating dry eye." *Id.*

19. Claim 26 of the '111 patent states "[t]he topical ophthalmic emulsion of claim 18, wherein the topical ophthalmic emulsion is therapeutically effective in treating keratoconjunctivitis sicca." *Id.*

20. The Court construed the term "keratoconjunctivitis sicca" to mean "a type of dry eye disease involving an absolute or partial deficiency in aqueous tear production." Doc. No. 214 at 13.

21. The Court construed the terms "dry eye," "dry eye disease," and "dry eye syndrome" to mean "a disorder of the tear film due to reduced tear production or excessive tear

evaporation that is associated with ocular discomfort and/or visual symptoms and may cause disease of the ocular surface."[4] *Id.*

22. The Court construed the term "restoring [lacrimal gland] tearing" to mean "returning the quantity and/or quality of tearing, in whole or in part, to a prior, healthy state." *Id.* at 23. The Court also explained that restoring tearing "contemplate[s] that the patient's tear production will be returned to the status the patient enjoyed prior to the onset of the condition in question, or something close to it." *Id.* at 22-23.

23. In its original NDA, Allergan sought approval for the following proposed indication: "RESTASIS™ is indicated for the treatment of moderate to severe keratoconjunctivitis sicca; it restores and maintains normal tear secretion and ocular surface integrity while providing relief of symptoms associated with dry-eye." Ex. 1, AGN_RES0003896-4264 at 4103.

24. Allergan submitted Revised Draft Labeling to FDA on July 16, 1999, with a proposed indication that "RESTASIS™ is indicated for the treatment of moderate to severe keratoconjunctivitis sicca (chronic dry eye disease) to improve ocular surface health and relieve symptoms." Ex. 11, AGN_RES0064210-262 at 220.

25. On August 3, 1999, FDA sent a letter to Allergan finding that its NDA was "approvable" but could not be "approved" because, among other reasons, "the submitted studies are not replicative and are insufficient to establish efficacy in the treatment of moderate to severe keratoconjunctivitis sicca." Ex. 12, AGN_RES0064467-470 at 468.

[4] For ease of reference, when Defendants refer to "dry eye," Defendants refer to dry eye, dry eye disease, and dry eye syndrome collectively.

26. Allergan submitted a Response to Approvable Letter to FDA on December 8, 1999, with the proposed revised indication, "RESTASIS™ is indicated for the treatment of keratoconjunctivitis sicca (chronic dry eye disease) to improve tear production and relieve symptoms in patients whose disease is inadequately controlled with tear substitutes." Ex. 13, AGN_RES0064847-5192 at 5181 & 5165.
27. On March 25, 2000, FDA sent a second approvable letter stating "the submitted studies are not replicative and are insufficient to establish efficacy in the treatment of keratoconjunctivitis sicca (chronic dry eye disease) to improve tear production and relieve symptoms in patients whose disease is inadequately controlled with tear substitutes." Ex. 14, AGN_RES0065384-385 at 384.
28. Allergan submitted draft labeling to FDA on August, 22, 2000, again amending the proposed label to read: "RESTASIS™ is indicated for the treatment of moderate to severe keratoconjunctivitis sicca in patients with Sjögren's Syndrome or other autoimmune connective tissue disease. RESTASIS™ is also indicated for the treatment of moderate to severe keratoconjunctivitis sicca in post-menopausal women." Ex. 15, AGN_RES0065649-662 at 653 & 656.
29. On October 19, 2000, FDA sent a third approvable letter stating that the NDA could not be approved because of the "lack of substantial evidence of efficacy…[s]pecifically, the submitted studies are not replicative and are insufficient to establish efficacy in the treatment of keratoconjunctivitis sicca (chronic dry eye disease) to improve tear production and relieve symptoms in patients whose disease is inadequately controlled with tear substitutes" and substantial evidence did not support that "the drug product will have the effect it purports or is represented to have under the conditions of use

prescribed, recommended or suggested in the proposed labeling." Ex. 16, AGN_RES0065782-783 at 782.

30. On April 23, 2002, Allergan submitted another Clinical Amendment proposing an indication section that read, "…indicated for patients with moderate to severe *keratoconjunctivitis sicca* (dry eye disease) to increase tear production"). Ex. 17, AGN_RES0065830-905 at 835 (emphasis in original).

31. On May 22, 2002, Allergan submitted an Amendment to FDA with the proposed indication, "RESTASIS™ is indicated for the treatment of moderate to severe keratoconjunctivitis sicca." Ex. 18, AGN_RES0065908-935 at 914.

32. On November 15, 2002, Allergan submitted a Clinical Amendment, with revised draft labeling to FDA stating, "RESTASIS™ is indicated to increase tear production in patients with moderate to severe keratoconjunctivitis sicca." Ex. 19, AGN_RES0066841-940 at 850 & 856.

33. On December 13, 2002, FDA responded to Allergan's Restasis® draft labeling and proposed the following: "RESTASIS™ is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation. Increased tear production in these patients is limited to those not currently taking anti-inflammatory drugs or using punctal plugs." Ex. 20, AGN_RES0067040-048 at 042.

34. On December 13, 2002, Allergan responded to FDA, via fax, with a "minor request for change to indication" and added a handwritten change to the indication, thus proposing, "RESTASIS™ is indicated to increase tear production in patients ***with dry eye*** whose tear production is presumed to be suppressed due to ocular inflammation. Increased tear

production in these patients is limited to those not currently taking anti-inflammatory drugs or using punctal plugs." Ex. 21, AGN_RES0067049-50 (emphasis added).

35. Allergan submitted a formal Labeling Amendment on December 16, 2002, which did not include the "with dry eye" language formerly proposed in the indication. Instead, Allergan proposed the following: "RESTASIS™ is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation. Increased tear production in these patients is limited to those not currently taking anti-inflammatory drugs or using punctal plugs." Ex. 22, AGN_RES0067051-064 at 058.

36. On December 20, 2002, Allergan submitted another Labeling Amendment, with the final proposed indication reading, "RESTASIS™ is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca. Increased tear production was not seen in patients currently taking topical anti-inflammatory drugs or using punctal plugs." Ex. 23, AGN_RES0067066-080 at 072.

37. On December 23, 2002, FDA approved Restasis® for the indication Allegan proposed in its December 20, 2002 Labeling Amendment. Ex. 24, AGN_RES0067081-088 at 084.

38. Each of Defendants' proposed ANDA labels mirror the Restasis® label and recite the same indication as Restasis®. Exs. 25-29.

IV. LEGAL STANDARDS

Summary judgment is appropriate if the evidence "show[s] that there is no genuine issue as to any material fact and that the moving party is entitled to a judgment as a matter of law." *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1354 (Fed. Cir. 2003) (quoting Fed. R. Civ. P. 56(c)). "The evidence of the nonmovant is to be believed, and all justifiable inferences

are to be drawn in his favor." *Id.* (quoting *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 255 (1986)).

"[I]t is not an act of infringement to submit an ANDA for approval to market a drug for a use when . . . the patent at issue is for a use not approved under the NDA." *Id.* at 1354-55. In other words, "because an ANDA may not seek approval for an unapproved or off-label use of a drug under 21 U.S.C.§ 355(j)(2)(A)(i), it necessarily follows that 35 U.S.C. § 271(e)(2)(A) does not apply to a use patent claiming only such a use." *Bayer Schering Pharma AG v. Lupin, Ltd.*, 676 F.3d 1316, 1319 (Fed. Cir. 2012) (quoting *Warner-Lambert*, 316 F.3d at 1356).

V. ARGUMENT

The basic facts underlying this motion are not in dispute: the only FDA-approved indication for Restasis® is to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with KCS. Allergan repeatedly sought, but failed to obtain FDA approval of an indication for treating moderate to severe KCS and dry eye. Restasis® is not FDA-approved to treat dry eye or KCS, nor is it approved to restore tearing to a prior healthy state.

The Federal Circuit, interpreting FDA regulations, has explained that the FDA-approved "use" of a pharmaceutical product is set forth in the "Indications and Usage" section of a drug label. *Bayer*, 676 F.3d at 1322-23 (explaining that (1) the only FDA-approved uses of a drug are present in the "Indications and Usage" section; (2) other indications and uses "must not be implied or suggested in other sections of the labeling if not included in this section"; and (3) "indications set forth in that section [must] be supported by 'substantial evidence of effectiveness based on adequate and well-controlled studies.'") (quoting 21 C.F.R. § 201.57(c)(2)(iv)). This principal holds "even though [the relevant drug product] necessarily had those [therapeutic] effects in patients who took the drug for the approved purpose." *Bayer*, 676 F.3d at 1321. Thus, assuming *arguendo* that Restasis® has the effect of treating dry eye and KCS and restoring tearing to a prior healthy state, Defendants cannot infringe claims directed to these methods of

use and efficacy conditions because FDA has not approved Restasis® for anything but to increase tear production.

Defendants do not and cannot seek FDA approval for any indication other than the FDA-approved indication for Restasis®. The Federal Circuit has held that an ANDA applicant cannot infringe a patent claim that recites a use or method of treatment different from the FDA-approved indication. Accordingly, as a matter of law, Defendants cannot directly or indirectly infringe asserted claims that recite uses for treating dry eye or KCS or uses for restoring tearing—uses for which Defendants do not seek FDA approval (nor have they been approved by FDA). *See, e.g.*, *Bayer*, 676 F.3d at 1326 (holding that defendants cannot be held liable for infringement of patent claims directed to producing contraceptive, anti-mineralocorticoid, and anti-androgenic effects when the ANDA sought approval to market solely for contraceptive use); *Allergan, Inc. v. Alcon Labs., Inc.*, 324 F.3d 1322, 1334 (Fed. Cir. 2003) (affirming summary judgment of noninfringement because defendants "are not seeking FDA approval for the uses claimed in the patents and because the uses claimed in the patents are not FDA-approved"); *Warner-Lambert*, 316 F.3d at 1352, 1362 (affirming summary judgment of noninfringement for generic drug seeking FDA-approval for method of treating epilepsy when patent directed to method of treatment of neurodegenerative diseases).

A. RESTASIS® WAS APPROVED BY FDA ONLY FOR THE INDICATION SPECIFIED IN THE RESTASIS® LABEL

1. The Only FDA-Approved Indication and Usage for Restasis® is to Increase Tear Production in Patients Whose Tear Production is Presumed to Be Suppressed Due to Ocular Inflammation Associated with KCS

The "Indications and Usage" section of Allergan's Restasis® label states that "Restasis® ophthalmic emulsion is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca. Increased tear production was not seen in patients currently taking topical anti-inflammatory drugs or using punctal plugs." Ex. 4. AGN_RES0069704-709 at 705. This is the only FDA-

approved indication for Restasis®. Both Allergan's and Defendants' experts agree on this point. Ex. 30, Perry Dep. at 114:1-22; Ex. 3, Noecker Dep. at 18:2-19:8; Fleischer Dec. at ¶¶ 29, 30, 35, 40, 41. It is undisputed that FDA did not approve Restasis® to treat KCS, a type of dry eye disease. Ex. 3, Noecker Dep. at 133:22-134:5.

Allergan's expert on infringement, Dr. Robert Noecker, admits (as he must) that the words "dry eye" do not appear in the "Indications and Usage" portion of the Restasis® label. *Id.* at 22:7-10. In addition, Defendants' FDA expert, Dr. Fleischer, explains that the regulatory correspondence between Allergan and FDA during the approval process reflects the specific language appearing in the Restasis® label in the "Indications and Usage" section. Fleischer Dec. at ¶¶ 11-29. That is, FDA approved Restasis® for the indication on the label and nothing more. *Id.* at ¶¶ 29, 30, 33, 35, 40, 41. Thus, it is inaccurate—both as a matter of FDA regulation and law—to state that Restasis® is indicated for the treatment of dry eye or KCS or to restore tearing to a prior healthy state. Accordingly, Restasis® is not properly indicated to treat dry eye or KCS or restore tearing, as is recited in claims 13, 14, and 24 of the '162 patent; claims 12, 13, 16, 22, 26 and 27 of the '191 patent; claims 11 and 18 of the '556 patent; and claims 17, 25, and 26 of the '111 patent. Fleischer Dec. at ¶¶ 33, 38, 40; Calman Dec. at ¶¶ 23-25, 35.

2. FDA Did Not Approve Restasis® to Treat Dry Eye or KCS or to Restore Tearing and Allergan Unsuccessfully Tried to Establish Therapeutic Efficacy in Treating KCS and Dry Eye

It is undisputed that the label for Restasis® does not reflect FDA approval to treat KCS, which is a subset of dry eye. Ex. 3, Noecker Dep. at 133:22-134:5; Calman Dec. at ¶¶ 23-25, 35; Fleischer Dec. at ¶¶ 29, 33; Doc. No. 214 at 13. It follows, then, that Restasis® is not FDA-approved to treat the full range of dry eye disorders encompassed by the term "dry eye." Doc. No. 214 at 13; Calman Dec. at ¶¶ 33-34. Nor is Restasis FDA-approved to restore tearing to some prior, healthy state. *Id.* at ¶¶ 23-24, 31; Fleischer Dec. at ¶¶ 34-35. The FDA-approved indication is simply narrower than, and does not cover, such treatments or uses.

The language used in the Restasis® "Indications and Usage" section is not susceptible to another interpretation because Allergan actually sought an indication for treating KCS and was denied approval for lack of substantial evidence of effectiveness based on adequate and well-controlled studies. Fleischer Dec. at ¶¶ 11-29. Specifically, Allergan initially sought FDA-approval for the treatment of KCS and chronic dry eye. *Id.* at ¶¶ 11-12, 15, 17, 35; Ex. 1, AGN_RES0003896-4264 at 4103. FDA denied approval for those indications because Allergan failed to show that Restasis® was therapeutically effective at treating those disorders. Fleischer Dec. at ¶¶ 13, 16, 20. After reviewing Allergan's Phase 2 and Phase 3 clinical trial data, FDA found that the studies "were insufficient to establish efficacy in the treatment of" moderate to severe KCS (Ex. 12, AGN_RES0064467-470 at 468) and chronic dry eye disease (Ex. 14, AGN_RES0065384-385 at 384). *See also* Ex. 16, AGN_RES0065782-783 at 782. Allergan's infringement expert, Dr. Noecker, does not dispute that FDA concluded that Allergan's clinical data was insufficient. Ex. 3, Noecker Dep. at 126:25-128:13. Nor does Dr. Noecker dispute that FDA did not approve Restasis® for restoring tearing to some prior, healthy state, as is required by this Court's construction of the term "restoring [lacrimal gland] tearing." Doc. No. 214 at 23; Ex. 3, Noecker Dep. at 18:2-19:8; 133:22-134:5; *see also* 106:2-6.

3. As a Matter of Law, the "Indications and Usage" Section of the Label Governs and Does Not Reflect Any Therapeutic Use For Treatment of KCS, Dry Eye, or Restoring Tearing

Even if doctors prescribe Restasis® for "off-label" uses, *i.e.*, uses other than what is indicated on the label, it does not follow that Restasis® is FDA-approved as safe and effective for those uses. Fleischer Dec. at ¶¶ 35-38; Calman Dec. at ¶ 24 . As a matter of law, nothing in the Restasis® label can properly imply or suggest that Restasis® is FDA-approved as safe and effective for treating dry eye or KCS or for restoring tearing. 21 C.F.R. § 201.57(c)(2)(iv) (stating that indications must be supported by safety and efficacy data and "[i]ndications or uses must not be implied or suggested in other sections of the labeling if not included in [the Indications and Usage] section"); *accord Bayer*, 676 F.3d at 1323; *Warner-Lambert*, 316 F.3d at

1356. This is true notwithstanding any non-FDA approved use codes that Allergan may have listed for Restasis® in the Orange Book. *See Bayer*, 676 F.3d at 1324-35.

Consistent with the "Indication and Usage" on the Restasis® label, the "Clinical Studies" portion narrowly describes the results in terms of Schirmer wetting, which is undisputedly a measure of tear production. Ex. 3, Noecker Dep. at 95:10-20; 97:16-21; 99:2-9; Calman Dec. at ¶¶ 13, 28, 32. Based on the outcomes reported in increased Schirmer scoring in its Phase 3 clinical trials, Allergan submitted a series of clinical amendments to FDA advocating that Schirmer scores "by themselves, are a clinically relevant endpoint." Fleischer Dec. at ¶ 21. In response to Allergan's new focus on Schirmer scoring, FDA suggested that Allergan modify the indication from the "treatment of moderate to severe keratoconjunctivitis sicca" to "increas[ing] tear production." Fleischer Dec. at ¶¶ 21-25. Thus, the final indication appearing on the label for Restasis® reflects the measure (Schirmer scoring) used to evaluate the efficacy of Restasis®. The regulatory history shows that Allegan's clinical trials did not establish that Restasis® is effective at treating KCS. Dr. Noecker does not dispute that this is what FDA found. Ex. 3, Noecker Dep. at 126:25-127:17; *see also* 133:12-20. Nor can Allergan ignore this distinction or the scope of its FDA-approved indication.

Restoring tearing does not mean the same thing as increasing tear production. The Court construed "restoring [lacrimal gland] tearing" to mean "returning the quantity and/or quality of tearing, in whole or in part, to a prior, healthy state." Doc. No. 214 at 23. Nothing in the FDA-approved indication states or implies that use of Restasis® will return a patient to the status of tearing held prior to the onset of KCS, dry eye, or dry eye disease. Calman Dec. at ¶¶ 31-32, 35. It is undisputed that Allergan's Phase 3 clinical trials did not attempt to measure a patient's prior, healthy state as a baseline to evaluate whether tearing was restored because every patient in Allergan's clinical trials was eligible only if they initially had a diagnosis of moderate to severe dry eye disease. Ex. 31, Sall *et al.*, "Two Multicenter, Randomized Studies of the Efficacy and Safety of Cyclosporin Ophthalmic Emulsion in Moderate to Severe Dry Disease," Ophthalmology, 107:631-639 (2000), COE_JDG_PriorArt_0000123-131 at 124; Calman Dec. at

¶¶ 31-32; *see also* Ex. 3, Noecker Dep. at 103:13-105:20; 108:8-109:21. In other words, patients participating in Allergan's clinical trials initially presented with a problem—a prior healthy state was never recorded. Thus, Restasis® is only indicated to increase tearing, not to restore tearing.

B. DEFENDANTS' PROPOSED ANDA LABELS SEEK APPROVAL FOR THE SAME INDICATION AND USAGE AS RESTASIS®

Pursuant to 21 U.S.C. § 355(j)(2)(A)(i), Defendants did not and cannot file ANDAs for unapproved uses. *Bayer*, 676 F.3d at 1319. Each Defendant filed an ANDA seeking approval for a cyclosporin ophthalmic emulsion, 0.05%, with proposed labels matching the indication for Restasis®. Exs. 25-29; Fleischer Dec. at ¶¶ 31, 41; Calman Dec. at ¶¶ 20, 36. Defendants do not seek approval for products to treat KCS, dry eye, or restore tearing, and therefore, Defendants cannot be liable for infringement of any of these unapproved uses. *Bayer*, 676 F.3d at 1319 (holding that an "infringement claim . . . lies only against a patented use that has been approved by the FDA."); *see also* Calman Dec. at ¶ 37.

Even if, as Allergan contends, Defendants' respective ANDA products have the ultimate effects of treating KCS, dry eye, dry eye disease, or restoring lacrimal gland tearing (despite FDA's lack of approval for Restasis®), Defendants are not liable under the Hatch-Waxman Act for infringing claims reciting those unapproved uses. *See* Fleischer Dec. at ¶ 42. The Federal Circuit has upheld this legal principle. For example, in *Allergan, Inc. v. Alcon Laboratories, Inc.*, the generic manufacturer sought approval for a generic brimonidine product for the FDA-approved use of reducing intraocular pressure. 324 F.3d at 1324. Allergan asserted that the generic manufacturer infringed two patents that claimed methods of protecting the optic nerve and neural protection, uses for which brimonidine was effective. *Id.* But the patented uses of brimonidine were not FDA-approved. The Federal Circuit concluded that the generic manufacturer could not be liable for infringement "even though brimonidine necessarily had those protective effects in patients who took the drug for the approved purpose." *Bayer*, 676 F.3d at 1321 (interpreting *Allergan*, 324 F.3d at 1324).

Thus, as a matter of law under the Hatch-Waxman Act, Defendants cannot infringe claims 13, 14, and 24 of the '162 patent; claims 12, 13, 16, 22, 26 and 27 of the '191 patent; claims 11 and 18 of the '556 patent; and claims 17, 25, and 26 of the '111 patent because they recite a use other than the FDA-approved indication for Restasis®.

C. DEFENDANTS' LABELS DO NOT INDUCE INFRINGEMENT AND THERE ARE SUBSTANTIAL NONINFRINGING USES

Allergan has alleged that Defendants will induce or contribute to the infringement of claims reciting unapproved uses based on their proposed ANDA product labeling. For substantially the same reasons discussed above with respect to direct infringement, Defendants cannot be liable for induced or contributory infringement of those claims.[5] *See* Calman Dec. at ¶ 41.

First, Allergan contends that doctors and patients will directly infringe these claims if they use Defendants' ANDA products "in a manner consistent with its proposed label." *E.g.*, Ex. 2, Mylan Noecker Report at ¶ 672. But "a method of use patent holder may not sue an ANDA applicant for induced infringement of its patent, if the ANDA applicant is not seeking FDA approval for the use claimed in the patent and if the use claimed in the patent is not FDA-approved." *Allergan*, 324 F.3d at 1332 (citation omitted). Thus, Allergan's allegation of inducement lacks the predicate act of direct infringement.

Setting aside the lack of direct infringement, Defendants' proposed labels do not include indications for treating dry eye or KCS or restoring tearing. Calman Dec. at ¶¶ 41-42. These are not FDA-approved uses for Restasis®, and Defendants do not seek approval for them. *Id.* at ¶¶

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[5] Potential infringement under 35 U.S.C. § 271(e)(2) includes induced and contributory infringement arising from the sale or method of using a drug for which an ANDA has been filed. *Warner Lambert*, 316 F.3d at 1365-66 ("[T]he substantive determination of whether actual infringement or inducement will take place [by the ANDA filer] is determined by traditional patent infringement analysis, just the same as it is in other [non-ANDA] infringement suits . . . ."); *see also Wyeth v. Sandoz, Inc.*, 703 F.Supp.2d 508, 522 (E.D. N.C. 2010) ("Where an ANDA is involved, contributory infringement claims may be brought under section 271(e)(2) . . . .") (citing *Allergan, Inc.*, 324 F.3d at 1331).

35-37, 41. Therefore, even if it were considered an act of direct infringement to use the proposed ANDA products to treat dry eye or KCS or to restore tearing, Defendants' labels are not evidence of an affirmative intent to induce doctors and patients to perform the unapproved uses. Exs. 25-29.

Accordingly, Defendants' proposed ANDA labels cannot induce doctors or patients to directly infringe claims 13, 14, and 24 of the '162 patent; claims 12, 13, 16, 22, 26 and 27 of the '191 patent; claims 11 and 18 of the '556 patent; and claims 17, 25, and 26 of the '111 patent.

Second, Defendants do not contribute to infringement of these claims. Again, Allergan's allegation lacks the predicate of direct infringement. *See Endo Pharms. Inc. v. Amneal Pharms., LLC*, 12 Civ. 8115 (TPG), 2015 U.S. Dist. LEXIS 114816, at *93 (S.D.N.Y. Aug. 18, 2015) (citing *Fujitsu Ltd. v. Netgear Inc.*, 620 F.3d 1321, 1326 (Fed. Cir. 2010) (finding generic manufacturer does not contributorily infringe certain claims because there is no direct infringement).

In any event, the claimed ophthalmic emulsions have substantial noninfringing uses that preclude a finding of contributory infringement. Off-label uses of Restasis®, *e.g.*, to treat dry eye or KCS, are substantial uses that cannot infringe because those uses are not FDA-approved. It is not disputed that Restasis® is prescribed by clinicians for uses not specified in the "Indications and Uses" section of the Restasis® label, *e.g.*, for treating dry eye or KCS. Ex. 3, Noecker Dep. at 18:15-19:15; 29:20-30:4; 38:15-39:7; 50:19-51:4; Calman Dec. at ¶¶ 43-44.

Because of these substantial, non-infringing, off-label uses, Defendants do not contribute to infringement of claims 13, 14, and 24 of the '162 patent; claims 12, 13, 16, 22, 26 and 27 of the '191 patent; claims 11 and 18 of the '556 patent; and claims 17, 25, and 26 of the '111 patent.

VI. CONCLUSION

For the foregoing reasons, Defendants respectfully request that the Court grant partial summary judgment of noninfringement of claims 13, 14, and 24 of the '162 patent; claims 12,

13, 16, 22, 26 and 27 of the '191 patent; claims 11 and 18 of the '556 patent; and claims 17, 25, and 26 of the '111 patent. There is no dispute that Restasis® is indicated for only one use approved by FDA—to increase tear production, not to treat KCS, dry eye, or restore tearing. Defendants do not, and cannot, seek approval from FDA to market cyclosporin ophthalmic emulsions, 0.05%, for any indication except to increase tear production. Therefore, both the undisputed facts of this case and the law support a finding of noninfringement of the asserted claims directed to the treatment of KCS, dry eye, and restoring tearing.

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Respectfully submitted,

/s/ *Anna G. Phillips*

Douglas Carsten
Email: dcarsten@wsgr.com
Wendy Devine
Email: wdevine@wsgr.com
Christina Dashe
Email: cdashe@wsgr.com
WILSON SONSINI GOODRICH & ROSATI
12235 El Camino Real, Suite 200
San Diego, CA 92130-3002
Phone: (858) 350-2300
Fax: (858) 350-2399

Anna G. Phillips (TX Bar No. 24090329)
WILSON SONSINI GOODRICH & ROSATI
900 South Capital of Texas Highway
Las Cimas IV, Fifth Floor
Austin, TX 78746-5546
Phone: (512) 338-5400
Fax: (512) 338-5499
anphillips@wsgr.com

Melissa Smith
GILLAM & SMITH LLP
303 S. Washington Ave.
Marshall, Texas 75670
Tel. 903.934.8450
Fax 903.934.9257
melissa@gillamsmithlaw.com

COUNSEL FOR DEFENDANTS MYLAN PHARMACEUTICALS INC. AND MYLAN INC.

/s/ *J.C. Rozendaal*
J.C. Rozendaal (*pro hac vice*)
Michael E. Joffre (*pro hac vice*)
Pauline M. Pelletier (*pro hac vice*)
R. Wilson Powers III (*pro hac vice*)
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 New York Ave. NW, Suite 600
Washington, DC 20005
Tel: 202-371-2600
Fax: 202-371-2540
jcrozendaal@skgf.com
mjoffre@skgf.com
ppelletier@skgf.com
tpowers@skgf.com

Louis B. ("Brady") Paddock
Texas Bar No. 00791394
NIX, PATTERSON & ROACH L.L.P.
2900 St. Michael Drive, Ste. 500
Texarkana, TX 75503
(903) 223-3999
(903) 223-8520 (fax)
bpaddock@nixlawfirm.com

COUNSEL FOR DEFENDANT TEVA PHARMACEUTICALS USA, INC.

/s/ *Stephen R. Smerek*
Stephen R. Smerek (*pro hac vice*)
Shilpa Coorg (*pro hac vice*)
Jason Craig Hamilton (*pro hac vice*)
WINSTON & STRAWN LLP
333 South Grand Avenue, 38th Floor
Los Angeles, CA 90071-1543
Tel: 213-615-1933
Fax: 213-615-1750
ssmerek@winston.com
scoorg@winston.com
jhamilton@winston.com

Charles B. Klein (*pro hac vice*)
WINSTON & STRAWN LLP
1700 K Street, NW
Washington, DC 20006
Tel: 202-282-5977
Fax: 202-282-5100
cklein@winston.com

Deron R. Dacus
Peter Aaron Kerr
THE DACUS FIRM, PC
821 ESE Loop 323, Suite 430
Tyler, TX 75701
Tel: 903-705-1117
Fax: 903-581-2543
ddacus@dacusfirm.com
pkerr@dacusfirm.com

COUNSEL FOR DEFENDANT INNOPHARMA, INC.

/s/ *Peter J. Curtin*

William A. Rakoczy (pro hac vice)
Paul J. Molino (pro hac vice)
Peter J. Curtin (pro hac vice)
John D. Polivick (pro hac vice)
Kevin P. Burke (pro hac vice)
Patrick N. Abbott (pro hac vice)
RAKOCZY MOLINO MAZZOCHI SIWIK LLP
6 West Hubbard Street, Suite 500
Chicago, Illinois 60654
Tel: (312) 222-6301
Fax: (312) 222-6321
wrakoczy@rmmslegal.com
paul@rmmslegal.com
pcurtin@rmmslegal.com
jpolivick@rmmslegal.com
kburke@rmmslegal.com
pabbott@rmmslegal.com

Eric H. Findlay
Texas Bar No. 00789886
Walter Wayne Lackey, Jr.
Texas Bar No. 24050901
FINDLAY CRAFT, P.C.

102 North College Avenue, Suite900
Tyler, TX 75702
Tel: (903) 534-1100
Fax: (903) 534-1137

COUNSEL FOR DEFENDANT FAMY CARE LIMITED

/s/ *Michael R. Dzwonczyk*

Michael R. Dzwonczyk
Mark Boland
Azy S. Kokabi
SUGHRUE MION, PLLC
2100 Pennsylvania Ave., N.W.
Washington, DC 20037
Telephone: (202) 293-7060
mdzwonczyk@sughrue.com
mboland@sughrue.com
akokabi@sughrue.com

E. Glenn Thames, Jr.
(Texas State Bar No. 00785097)
glennthames@potterminton.com
POTTER MINTON
A Professional Corporation
110 N. College Avenue, Suite 500
Tyler, TX 75702
Telephone: (903) 597-8311
Facsimile: (903) 593-0846

COUNSEL FOR DEFENDANT AND COUNTERCLAIM PLAINTIFF AKORN, INC.

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a true and correct copy of the above and foregoing document has been served on August 24, 2017 to all counsel of record who are deemed to have consented to electronic service via the Court's CM/ECF system per Local Rule CV-5(a)(3).

/s/ Melissa R. Smith